

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-73(Canceled).

74(Currently Amended). The composition according to claim ~~73~~ 160, which is a dimer comprising at least two independently modified peptides, wherein the R² of second one said modified peptide is attached to any amino acid the R² of the first other said modified peptide.

Claim 75(Cancelled).

76(Currently Amended). The composition according to claim ~~73~~ 160, comprising at least two said independently modified peptides wherein the second or additional one said modified peptides is attached to a branched construct of ~~the other~~ another said modified peptides in the composition.

Claims 77-78 (Cancelled).

79(Currently Amended). A method of treating a mammalian infection comprising administering to a mammal having said infection an ~~effective~~ amount of a peptide of claim ~~140~~ 140.

Claim 80(Canceled).

81(Currently Amended and Withdrawn). A method for identifying pharmaceutical compounds comprising:

- (i) performing a competitive assay with:
 - (a) a microorganism susceptible to a peptide of claim ±140;
 - (b) a peptide of claim ±140; and
 - (c) at least one test compound;
- (ii) exposing (a) to (b) and (c); and
- (iii) identifying said test compound which competitively displaces the binding of said peptide to a receptor on said microorganism.

82(Currently Amended). A pharmaceutical composition comprising one or more of the peptides of claim ±140 in a pharmaceutically acceptable carrier.

83(Currently Amended). A pharmaceutical composition comprising one or more of the compositions of claim ~~73~~ 160 in a pharmaceutically acceptable carrier.

84(Currently Amended). A The composition according to claim ~~73~~ 114, wherein R² of one said modified peptide is an alkanoic acid group and wherein ~~an additional~~ another said modified peptide is linked to the same R² ~~at the carboxyl terminus~~.

Claims 85-86 (Canceled).

87(Currently Amended). The peptide according to claim ±140, which is fused to a ~~second~~ protein.

Claims 88-89(Cancelled).

90(Currently Amended). The peptide according to claim ~~1~~141, wherein ~~said an additional amino acids of (d) or (e)~~have been cyclized is by the insertion into the structure of the an unnatural amino acid substituted with a ~~or~~ modifying sugars or imide.

91(Currently Amended). The peptide according to claim ~~1~~140, wherein said R¹ ~~group (d) or (e)~~ is selected from the ~~additional amino acid residues group consisting of D-Val-, Arg-Val-, Lys-Val-, and Lys-Val-Asp-Lys-Val- SEQ ID NO: 5, and Arg-Pro-Pro-Thr-Pro-Arg-Pro-Leu-Lys-Val- SEQ ID NO: 3.~~

92(Currently Amended). The peptide according to claim ~~1~~140, wherein said R¹ ~~group (d) or (e)~~ is selected from the group consisting of Acetyl-Arg-Val-; Acetyl-Lys-Val-; and Acetyl-Lys-Val-Asp-Lys-Val- SEQ ID NO: 29.

93(Currently Amended). The peptide according to claim ~~1~~140, wherein said R¹ ~~group (c)~~ is biotin.

94(Currently Amended). The peptide according to claim ~~1~~140, wherein said R¹ ~~group (c)~~ is 5(6) carboxyfluorescein.

95(Currently Amended). The peptide according to claim ~~1~~140, wherein R¹ ~~group (c)~~ is radioactive.

96(Currently Amended). The peptide according to claim ~~1~~144, wherein R¹ ~~group (d) or (e) is a spacer interposed~~ is capable of bridging between the N- terminus and C-terminus of said peptide, ~~permitting cyclization of said peptide.~~

97(Currently Amended). The peptide according to claim 96, wherein R¹ ~~group (d) or (e)~~ is -Arg-Pro-Pro-Thr-Pro-Arg-Pro-Leu-Lys-Val- SEQ ID NO: 3, wherein said Val is

linked to the N-terminal Asp of ~~said formula~~ SEQ ID NO: 1 and the N-terminal amino acid of R¹ is linked by a covalent bond to the C-terminal amino acid of R².

98(Currently Amended). The peptide according to claim ~~+~~ 145, wherein said R¹ ~~group~~ (a) is 1-aminocyclohexane carboxylic acid.

99(Currently Amended). The peptide according to claim ~~+~~ 140, wherein said R¹ ~~group~~ provides a detectable signal, optionally upon interaction with other compounds.

100(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R² (e) is the amide of β -acetyl-2,3-diamino propionic acid.

101(Currently Amended). The peptide according to claim ~~+~~ 144, wherein R² (f) is a sequence of ~~four~~ 1 to 15 additional amino acids capable of cyclizing the modified peptide by bridging between the N- and C- termini ~~thereof~~ of said peptide.

Claim 102(Cancelled).

103(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R² (f) is selected from the group consisting of D-Asn, L-Asn, Asp, and Asn-R³, wherein R³ is a sugar.

104(Previously Presented). The peptide according to claim 103, wherein R³ is selected from the group consisting of 2-acetamido-2-deoxyglucose and triacetyl 2-acetamido-2-deoxyglucose.

105(Currently Amended). The peptide according to claim ~~+~~ 142, wherein at least one amino acid is a ~~altered to its corresponding~~ D amino acid.

106(Currently Amended). The peptide according to claim ~~1~~ 140, which is non-glycosylated.

107(Currently Amended). The peptide according to claim ~~1~~ 140, which is a cyclic peptide in which R^1 , R^2 , or a combination of R^1 and R^2 form an amino acid ~~spacer of greater than 3 amino acid residues~~ sequence of up to 15 amino acids in length capable of bridging the N- and C- termini of said peptide.

108(Currently Amended). The peptide according to claim 107, wherein said ~~spacer~~ sequence duplicates at least a portion of ~~the peptide sequence of claim 1~~ SEQ ID NO: 1.

109(Currently Amended). The peptide according to claim ~~1~~ 140, wherein at least one conventional amide bond between two amino acids in said sequence is replaced with a non-cleavable bond.

110(Previously Presented). The peptide according to claim 109, wherein said non-cleavable bond is a thio-amide bond or a reduced amide bond.

Claims 111-112 (Canceled).

113(Currently Amended). The composition according to claim ~~73~~ 143, comprising at least two said independently modified peptides, wherein at least one or more of said modified peptides is attached to a carrier.

114(Currently Amended). The composition according to claim ~~73~~ 160, which is a dimer comprising at least two independently modified peptides, wherein ~~each additional one modified peptide~~ one modified peptide is covalently linked to the R^2 of another modified peptide ~~in the composition.~~

115(Currently Amended). The composition according to claim ~~73~~ 160, which comprises a multiple antigenic peptide.

116(Previously Presented). The composition according to claim 115, wherein said multiple antigenic peptide comprises a β -alanine substituent on a poly-lysine core.

117(Previously Presented). The composition according to claim 115, comprising at least four peptides.

118(Currently Amended). ~~A~~ The composition according to claim ~~73~~ 114, wherein said R² amide of one of said independently modified peptides is comprises the amide of β -acetyl-2,3-diamino propionic acid ~~group~~ and wherein an additional modified peptide is linked to said amide at ~~the~~ its carboxyl terminus.

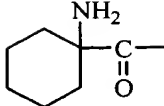
119(Currently Amended). The composition according to claim ~~73~~ 160, further comprising an amino acid or chemical compound ~~spacer~~ at the amino or carboxy termini of said modified peptides to link two or more said modified peptides together.

120(Currently Amended). The peptide according to claim ~~1~~ 140, wherein R¹ is Acetyl-Lys-Val-Asp-Lys-Val- SEQ ID NO: 29, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg,~~ and R² is Asn.

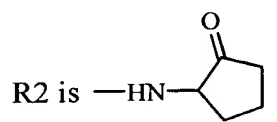
121(Currently Amended). The peptide according to claim ~~1~~ 140, wherein R¹ is Acetyl-Arg-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg,~~ and R² is Asn.

122(Currently Amended). The peptide according to claim ~~1~~ 140, wherein R¹ is Acetyl-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg,~~ and R² is Asn.

123(Currently Amended). The peptide according to claim ~~1~~ 140, wherein

R1 is , ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is Asn.

124(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R¹ is Acetyl-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and



125(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R¹ is Acetyl-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is NH-CH-CONH_2
 $\quad \quad \quad |$
 $\quad \quad \quad \text{CH}_2\text{-NH-COCH}_3$.

126(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R¹ is Acetyl-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is Asn-2-acetamido-2-deoxyglucose.

127(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R¹ is Acetyl-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is Asn-triacetyl-2-acetamido-2-deoxyglucose.

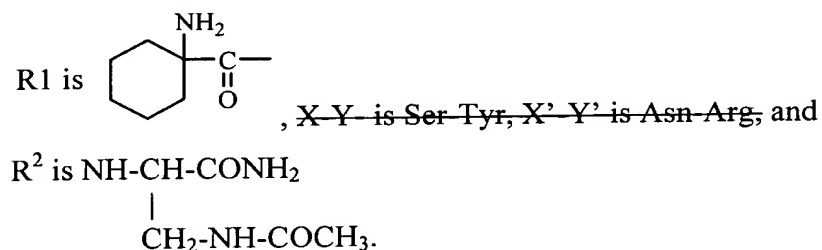
128(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R¹ is D-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is D-Asn.

129(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R¹ is Biotin-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is Asn.

130(Currently Amended). The peptide according to claim ~~+~~ 140, wherein R¹ is 5(6)-carboxyfluorescein-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is Asn.

131(Currently Amended). The peptide according to claim ~~1~~ 140, wherein R¹ is Acetyl-Lys-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is Asp.

132(Currently Amended). The peptide according to claim ~~1~~ 140, wherein



133(Currently Amended). The peptide according to claim ~~1~~ 140, wherein R¹ is Acetyl-Arg-Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is NH-CH-CONH₂

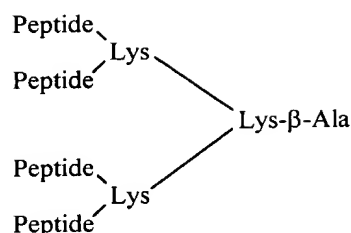


134(Currently Amended). The peptide according to claim ~~1~~ 140, wherein R¹ is Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is NH-CH-CONH₂

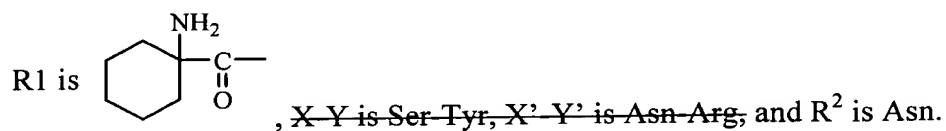


135(Currently Amended). The peptide according to claim 107, wherein R¹ is Val, ~~X-Y is Ser-Tyr, X'-Y' is Asn-Arg~~, and R² is Asn-Arg-Pro-Pro-Thr-Pro-Arg-Pro-Leu-Lys-, wherein the Lys group of R² is bound to Val of R¹.

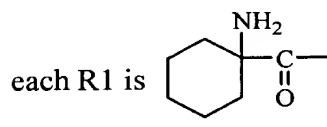
136(Currently Amended). The composition according to claim 117, comprising the structure



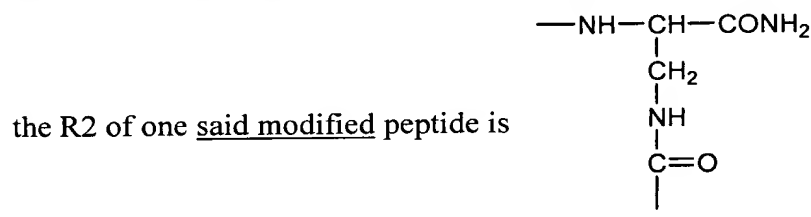
wherein each said peptide is of the formula R^1 ~~Asp-Lys-Gly-X-Y-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-X=~~ $Y=R^2$ SEQ ID NO: 1 $-R^2$, wherein:



137(Currently Amended). The composition according to claim 74, comprising two said modified peptides of SEQ ID NO: 1 linked at their R^2 ~~moieties-~~ groups, wherein:



~~each X-Y is Ser-Tyr, each X'-Y' is Asn-Arg, and wherein~~



and the R^2 of the ~~second~~ other said modified peptide is $-CH-CH_2-NH-COCH_3$.

138(Currently Amended). The composition according to claim 136, wherein said multiple antigenic peptide is produced synthetically or recombinantly.

139(Currently Amended). The composition according to claim 136, wherein one or more of said modified peptides is a synthetic peptide fused to a ~~second moiety, wherein~~ said moiety peptide sequence, protein or chemical compound that enhances the bioavailability of said modified peptides.

140(New): A modified pyrrhocoricin peptide of the formula R^1 -SEQ ID NO: 1- R^2 having anti-bacterial activity,

wherein SEQ ID NO: 1 is -Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg- ,

wherein said Thr in SEQ ID NO: 1 lacks the glycosylation of the Thr residue of naturally-occurring pyrrhocoricin;

wherein said Ser-Tyr amino acids and said Asn-Arg amino acids in said SEQ ID NO: 1 are independently selected from the group consisting of naturally-occurring amino acids and unnatural amino acids that improve the stability of the bond between the Ser-Tyr or Asn-Arg amino acids against protease degradation;

wherein R^1 adds a net positive charge to the N-terminus of said peptide and is selected from the group consisting of

- (a) a straight chain, branched, cyclic or heterocyclic alkyl group;
- (b) a straight chain, branched, cyclic or heterocyclic alkanoyl group;
- (c) a positively charged reporter group; and
- (d) a sequence consisting of between 1 to 15 additional amino acids,

wherein said additional amino acids are optionally substituted by one or more of (a), (b), or (c); and wherein said additional amino acids are capable of cyclizing the peptide by bridging between the N- and C-termini thereof; and

wherein R^2 is selected from the group consisting of

- (e) a free hydroxyl, an amide, an imide, or a sugar;
- (f) a sequence consisting of 1 to 15 additional amino acids, wherein

said additional amino acids are optionally substituted by a free hydroxyl, an amide, an imide, or a sugar; and wherein said additional amino acids optionally cyclize the peptide by bridging between the N- and C- termini thereof.

141(New): The peptide according to claim 140 wherein said additional amino acids of (d), and (f) are independently selected from naturally-occurring or unnatural amino acids.

142(New): The peptide according to claim 141, wherein said unnatural amino acids are selected from the group consisting of a D-amino acid, a diaminocarboxylic acid, an amide of a diaminocarboxylic amide group and an amino cycloalkane carboxylic acid.

143(New): The peptide according to claim 140, wherein R^1 (d) is a sequence consisting of between 1 to 15 additional amino acids, which comprises a portion of SEQ ID NO: 1.

144(New): The peptide according to claim 132, wherein R^1 (d) comprises -Arg-Pro-Pro-Thr-Pro-Arg-Pro-Leu-Lys-Val- SEQ ID NO: 3.

145(New): The peptide according to claim 140, wherein R^1 (a) is 1-aminocycloalkane carboxylic acid.

146(New): The peptide according to claim 140, wherein R^1 (a) is a cyclic or heterocyclic alkyl or alkanoyl group.

147(New): The peptide according to claim 146, wherein R^1 (a) is an n-amino-n-carboxy cyclic alkyl or alkanoyl group.

148(New): The peptide according to claim 140, wherein R^1 (f) is a sequence consisting of between 1 to 15 additional amino acids, which comprises a portion of SEQ ID NO: 1.

149(New): The peptide according to claim 148, wherein said portion of SEQ ID NO: 1 is in C-terminal to N-terminal order.

150(New): The peptide according to claim 149, wherein said portion is -Arg-Pro-Pro-Thr-Pro-Arg-Pro-Leu-Lys-Val- SEQ ID NO: 3.

151(New): The peptide according to claim 101, wherein an additional amino acid of R^2 (f) is an unnatural amino acid.

152(New): The peptide according to claim 148, wherein an additional amino acid of R^2 (f) is an unnatural amino acid.

153(New): The peptide according to claim 151, wherein said unnatural amino acid is a diaminocarboxylic acid or an amide of a diaminocarboxylic acid.

154(New): The peptide according to claim 152 wherein said unnatural amino acid is a diaminocarboxylic acid or an amide of a diaminocarboxylic acid.

155(New): The peptide according to claim 140, wherein said R^2 (f) is a sequence consisting of from 1 to 15 additional amino acids, wherein said additional amino acids are selected from the group consisting of an Asn, a diaminocarboxylic acid, an amide of a diaminocarboxylic acid, a sequence of amino acids that duplicate at least a portion of SEQ ID NO: 1, and combinations thereof.

156(New): The peptide according to claim 140, wherein said Ser-Tyr amino acids in SEQ ID NO: 1 are linked by a protected amide bond.

157(New): The peptide according to claim 156 wherein said protected amide bond is selected from the group consisting of a reduced amide bond and a thioamide bond.

158(New): The peptide according to claim 140, wherein said Asn-Arg amino acids in SEQ ID NO: 1 are linked by a protected amide bond.

159(New): The peptide according to claim 158, wherein said protected amide bond is selected from the group consisting of a reduced amide bond, and a thioamide bond.

160(New): A multivalent composition having anti-bacterial activity and comprising at least two modified pyrrocoricin peptides, each peptide having the formula R^1 -SEQ ID NO: 1- R^2 ,

wherein SEQ ID NO: 1 is -Asp-Lys-Gly-Ser-Tyr-Leu-Pro-Arg-Pro-Thr-Pro-Pro-Arg-Pro-Ile-Tyr-Asn-Arg- ,

wherein said Thr in SEQ ID NO: 1 lacks the glycosylation of the Thr residue of naturally-occurring pyrrocoricin;

wherein said Ser-Tyr amino acids and said Asn-Arg amino acids in said SEQ ID NO: 1 are independently selected from the group consisting of naturally-occurring amino acids and unnatural amino acids that improve the stability of the bond between the Ser-Tyr or Asn-Arg amino acids against protease degradation;

wherein R^1 adds a net positive charge to the N-terminus of said peptide and is selected from the group consisting of

- (a) a straight chain, branched, cyclic or heterocyclic alkyl group;
- (b) a straight chain, branched, cyclic or heterocyclic alkanoyl group;
- (c) a positively charged reporter group; and
- (d) a sequence consisting of between 1 to 15 additional amino acids,

wherein said additional amino acids are optionally substituted by one or more of (a), (b), or (c); and wherein said additional amino acids are capable of cyclizing the peptide by bridging between the N- and C-termini thereof; and

wherein R^2 is selected from the group consisting of

- (e) a free hydroxyl, an amide, an imide, or a sugar;
- (f) a sequence consisting of 1 to 15 additional amino acids, wherein

said additional amino acids are optionally substituted by a free hydroxyl, an amide, an imide, or a sugar; and wherein said additional amino acids are capable of cyclizing the peptide by bridging between the termini thereof.

161(New): The composition according to claim 160, wherein said Ser-Tyr amino acids in SEQ ID NO: 1 are linked by a protected amide bond.

162(New): The composition according to claim 161, wherein said protected amide bond is selected from the group consisting of a reduced amide bond and a thioamide bond.

163(New): The composition according to claim 160, wherein said Asn-Arg amino acids in SEQ ID NO: 1 are linked by a protected amide bond.

164(New): The composition according to claim 163, wherein said protected amide bond is selected from the group consisting of a reduced amide bond and a thioamide bond.

165(New): The composition according to claim 160, wherein said additional amino acids of (d), and (f) are independently selected from naturally-occurring or unnatural amino acids.

166(New): The composition according to claim 161, wherein said unnatural amino acids are selected from the group consisting of a D-amino acid, a diaminocarboxylic acid, an amide of a diaminocarboxylic amide group and an amino cyclohexane carboxylic acid.

167(New): The composition according to claim 160, wherein R^1 (d) is capable of bridging between the free termini of said peptides.

168(New): The composition according to claim 160, wherein said R^1 (a) comprises a cyclic alkyl group.

169(New): The composition according to claim 160, wherein said R^1 (a) comprises a 1-aminocycloalkane carboxylic acid.

170(New): The composition according to claim 169, wherein said R^1 (a) comprises a 1-aminocyclohexane carboxylic acid.

171(New): The peptide according to claim 160, wherein R^1 (a) is a cyclic or heterocyclic alkyl or alkanoyl group.

172(New): The peptide according to claim 171, wherein R^1 (a) is an n-amino-n-carboxy cyclic alkyl or alkanoyl group.

173(New): The composition according to claim 160, wherein R^2 (f) is a sequence of 1 to 15 additional amino acids capable of cyclizing the peptides by bridging between the free termini of said peptides.

174(New): The composition according to claim 160, wherein an additional amino acid of R^2 (f) is an unnatural amino acid.

175(New): The composition according to claim 174, wherein said unnatural amino acid is a diaminocarboxylic acid or an amide of a diaminocarboxylic acid.

176(New): The composition according to claim 160, wherein said R^2 (f) is a sequence consisting of from 1 to 15 additional amino acids, wherein said additional amino acids are selected from the group consisting of an Asn, a diaminocarboxylic acid, an amide of a diaminocarboxylic acid, a sequence of amino acids that duplicate at least a portion of SEQ ID NO: 1, and combinations thereof.

177(New): The composition according to claim 160, wherein said R² (f) is a sequence consisting of from 1 to 15 additional amino acids, wherein said additional amino acids are selected from the group consisting of an Asn, a diaminopropanecarboxylic acid, an amide of a diaminopropane carboxylic acid, a sequence of amino acids that duplicate at least a portion of SEQ ID NO: 1, and combinations thereof.

178(New): The composition according to claim 160, which is non-glycosylated.

179(New): The composition according to claim 160, wherein at least one conventional amide bond between two amino acids in said sequence is replaced with a non-cleavable bond.

180(New): The composition according to claim 179, wherein said non-cleavable bond is a protected amide bond.

181(New): The composition according to claim 160, which comprises multiple copies of said modified peptide linked by attachment to one or more linked diaminocarboxylic acid groups.

182(New): The composition according to claim 181, wherein said diaminoacarboxylic acid group is a lysine.

183(New): The composition according to claim 182, wherein said diaminoacarboxylic acid group is further linked to a β -alanine substituent.

184(New): The composition according to claim 115, comprising a dimer of two modified peptides.

185(New): The composition according to claim 115, comprising three modified peptides.

186(New): A method of treating a mammalian infection comprising administering to a mammal having said infection an amount of a composition of claim 160.